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SYMPTOMATIC VERSUS ASYMPTOMATIC HYPOGLYCEMIA AMONG NEONATES ATTENDING NEONATAL CARE UNIT – COMPARATIVE STUDY CONDUCTED IN MOSUL-IRAQ

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ABSTRACT

Background: Hypoglycemia in neonate is a common but preventable metabolic disease that can lead to brain damage, mental retardation, and death. Despite an increase in hospital deliveries and improvements in neonatal care procedures, there are still disputes on the most effective method of detecting neonatal hypoglycemia, and it still happens frequently. Objectives: To compare the risk factors for symptomatic and asymptomatic hypoglycemia among neonates attending the neonatal intensive care unit. Methods: A comparative study was conducted, from January 2023 to the end of December 2023. The study was carried out in the Neonatal Intensive Care Unit at Ibin Al Atheer and Al Salam Teaching Hospitals in Mosul, Iraq. The study included both genders with blood glucose levels less than 45 mg/dL. Blood glucose levels greater than 45 mg/dL, congenital defects, and problems with feeding (such as cleft lip and palate) were excluded from the study. The questionnaire includes Three parts; part one for socio-demographic data such as patients' sex, maternal ages and parity. Part two for maternal obstetric history including gestational diabetes, pregnancy induced hypertension, premature rupture of membrane, use of oral hypoglycemic drugs and the presence of maternal metabolic diseases. Part three for neonatal factors such as birth weight, gestational age at birth (<37 weeks considered premature), and mode of delivery, furthermore; post-delivery complications such as birth asphyxia, neonatal sepsis, respiratory distress syndrome, hypothermia, endocrine disorder, inborn error of metabolism and inadequate feeding. Results: Among 160 patients enrolled in the study (80 with symptomatic and 80 with asymptomatic hypoglycemic patients), the majority of both groups are males, having mothers of less than 25 years and primigravida, delivered by normal vagina mode of delivery, premature and small for gestational age. It's evident that gestational diabetes is statistically significant different for patients with symptomatic hypoglycemia (P value <0.001). Moreover; the presence of small for gestational age was statistically significant different for patients with asymptomatic hypoglycemia (P value <0.049). Similarly; low birth weight was another factor found to be statistically significant for asymptomatic hypoglycemia (P value <0.041). Furthermore; respiratory distress syndrome was statistically significant for patients with asymptomatic hypoglycemia (P value <0.047). On the other hand; prematurity, appropriate for gestational age, large for gestational age, the presence of birth asphyxia, neonatal sepsis, hypothermia, endocrine disease, in born error of metabolism and inadequate feeding were shown to be statistically not significant between the two groups (P value more than 0.05) for all. Conclusion: According to the study findings; maternal GDM can cause more symptomatic hypoglycemia, while SGA, LBW, and RDS can caus asymptomatic hypoglycemia.

KEYWORDS: Newborn, Hypoglycemia, Mosul, Iraq.

1- INTRODUCTION

Hypoglycemia in neonate is a common but preventable metabolic disease that can lead to brain damage, mental

retardation, and death.^[1-2] Long-term effect of hypoglycemia may lead to Irreversible brain damage causing seizures and behavioral disorders.^[3] Symptoms

of the cerebral white matter atrophy, reduced myelination, and atrophic gyri might occur with hypoglycemia.^[4] The proper development and functioning of the nervous system depend on blood glucose.^[5] Small for gestational age (SGA) and preterm infants are more likely to have persistent hypoglycemia because they have an underdeveloped metabolic pathway at birth and insufficient liver glycogen and fat stores.^[6] Infants of diabetes mothers frequently have hyperinsulinemia and hypoglycemia.^[7]

There are several recognized causes for neonatal hypoglycemia, including insulin-secreting adenoma, congenital hypopituitarism, glycogen storage disorders, Beckwith-Wiedemann syndrome, islet cell dysregulation syndrome (nesidioblastosis), and abnormalities of amino acid metabolism.^[8] However; it has been difficult to diagnose hypoglycemia in infants since there isn't a clear correlation between plasma glucose levels, clinical symptoms, and long-term effects of hypoglycemia.^[9]

Hypoglycemia is defined as a glucose level two standard deviations below the population average.^[10] Healthy-term neonates rarely have serum glucose levels of 35 mg/dL within the first 3 hours of life, 40 mg/dL between 3-24 hours, and 45 mg/dL beyond 24 hours.^[11] Hormonal and metabolic changes in healthy full-term newborns guarantee that the important organs have a sufficient energy substrate in the early neonatal period following birth.^[12] However, preterm and small for gestational age newborns experience varied degrees of failure in this hormonal metabolic adaption after delivery.^[13]

Newborns with asymptomatic hypoglycemia may exhibit symptoms such as lethargy, jitteriness, apnea, irritability, and seizures.^[14] Treatment options vary based on the baby's birth weight and gestational age. Breastfeeding is the first line of defense against asymptomatic hypoglycemia. If blood glucose levels remain low, intravenous glucose may be necessary.^[15] Despite an increase in hospital deliveries and improvements in neonatal care procedures, there are still disputes on the most effective method of detecting neonatal hypoglycemia, and it still happens frequently.^[16] Therefore, the current study was conducted to compare the risk factors for symptomatic and asymptomatic

hypoglycemia among neonates attending the neonatal intensive care unit.

2-PATIENTS AND METHODS

Following permission from the Nineveh Health Directorate's ethical committee. From March 2024 until the end of March 2025, a comparative study was carried out in the Neonatal Intensive Care Unit at Ibin Al Atheer and Al Salam Teaching Hospitals in Mosul, Iraq. The study included both genders with blood glucose levels less than 45 mg/dL. Blood glucose levels greater than 45 mg/dL. congenital defects, and problems with feeding (such as cleft lip and palate) were excluded from the study.

The study included 80 neonates who were diagnosed with Symptomatic hypoglycemia (cases) and matched with 80 neonates with asymptomatic hypoglycemia which were collected from the same unit (controls).

The questionnaire includes Three parts; part one for socio-demographic data such as patients' sex, maternal ages and parity. Part two for maternal obstetric history including gestational diabetes, pregnancy induced hypertension, premature rupture of membrane, use of oral hypoglycemic drugs and the presence of maternal metabolic diseases. Part three for neonatal factors such as birth weight, gestational age at birth (<37 weeks considered premature), and mode of delivery, furthermore; post-delivery complications such as birth asphyxia, neonatal sepsis, respiratory distress syndrome, hypothermia, endocrine disorder, inborn error of metabolism and inadequate feeding.

Statistically analysis done by using SPSS 30.0 software application. To compare the means, the Student's t-test was employed. The p-value was considered statistically significant if it was less than 0.05.

3. RESULTS

Among 160 patients enrolled in the study (80 with symptomatic and 80 with asymptomatic hypoglycemic patients), the majority of both groups are males, having mothers of less than 25 years and primigravida, delivered by normal vagina mode of delivery, premature and small for gestational age. As shown in table 3.1.

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Variable	Sympton	matic=80	Asymptomatic=80		
	Number	Percent	Number	Percent	
Gender:					
-Male	44	55	41	51.25	
-Female	36	45	39	48.75	
Mother age:					
- Less than 25 years	61	76.25	65	81.25	
- More than 25 years	19	23.75	15	18.75	
Parity:					
-Multiparity	33	31.25	35	43.75	
-Primiparity	47	68.75	45	56.25	
Mode of delivery:					

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-Normal	51	63.75	46	57.5
-Cesarean section	29	36.25	34	42.5
Maturity:				
-Mature	22	27.5	27	33.75
-Premature	58	77.5	53	66.25
Gestational age:				
-Appropriate for gestational age	23	28.75	21	26.25
-Large for gestational age	9	11.25	7	8.75
-Small for gestational age	48	60	52	65

Table 3.2 shows comparison between patients with symptomatic and those with asymptomatic hypoglycemia according to their maternal factors. It's evident that gestational diabetes is statistically significant different for patients with symptomatic hypoglycemia (P value <0.001). while statistically no significant difference regarding pregnancy induced hypertension, preterm rupture of membrane, use of oral hypoglycemic drugs and the presence of metabolic disease (P value more than 0.05) for all.

Table 3.2: Comparison between patients with symptomatic and those with asymptomatic hypoglycemia according to their maternal factors.

Variable	Symptomatic=80		Asymptomatic=80		Divoluo
	Number	Percent	Number	Percent	r-value
Gestational diabetes:					
-Present	22	27.5	9	11.25	<0.001
-Absent	58	77.5	71	88.75	
Pregnancy induced hypertension:					
-Present	9	11.25	10	12.5	0.783
-Absent	71	88.75	70	87.5	
Premature rupture of membrane:					
-Present -Absent	4	5	3	3.75	0.689
	70	75	11	90.23	
Use of oral hypoglycemic drugs:					
-Present	6	7.5	5	6.25	0.502
-Absent	74	92.5	75	93.75	0.593
Metabolic disease:					
-Present	10	12.5	8	10	0.233
-Absent	70	87.5	72	90	0.235

Table 3.3 compares between patients with symptomatic and those with asymptomatic hypoglycemia regarding to their neonatal factors. It's evident that the presence of small for gestational age was statistically significant different for patients with asymptomatic hypoglycemia (P value <0.049). Moreover; low birth weight was another factor found to be statistically significant for asymptomatic hypoglycemia (P value <0.041). Furthermore; respiratory distress syndrome was statistically significant for patients with asymptomatic hypoglycemia (P value <0.047). On the other hand; prematurity, appropriate for gestational age, large for gestational age, the presence of birth asphyxia, neonatal sepsis, hypothermia, endocrine disease, in born error of metabolism and inadequate feeding were shown to be statistically not significant between the two groups (P value more than 0.05) for all.

Table 3.3: Comparison between patients with symptomatic and those with asymptomatic hypoglycemia according to their neonatal factors.

Variable	Symptomatic=80		Asymptomatic=80		D volue
	Number	Percent	Number	Percent	P-value
Prematurity:					
-Present	17	21.25	18	22.5	0.802
-Absent	63	78.75	62	77.5	0.892
Appropriate for gestational age:					
-Present					
-Absent	23	28.75	21	26.25	0.528

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	57	71.25	59	73.75	
Large for gestational:					
-Present	9	11.25	7	8.75	0.002
-Absent	71	88.75	73	91.25	0.095
Small for gestational age:					
-Present	48	60	52	70	0.040
-Absent	32	40	28	30	0.049
Low birth weight:					
-Present	15	13.75	24	30	0.041
-Absent	65	86.25	56	70	0.041
Birth Asphyxia:					
-Present	9	11.25	4	5	0.321
-Absent	71	88.75	76	95	0.321
Respiratory distress syndrome:					
-Present	17	21.25	29	36.25	0.047
-Absent	63	78.75	51	73.75	0.047
Neonatal sepsis:					
-Present	12	15	15	13.75	0.781
-Absent	68	85	65	86.25	0.781
Hypothermia:					
-Present	28	35	27	33.75	0.013
-Absent	52	65	53	66.25	0.915
Endocrine disease:					
-Present	6	7.5	1	1.25	0.138
-Absent	74	92.5	79	98.75	0.156
Inborn error of metabolism:					
-Present	4	5	7	8.75	0.489
-Absent	76	95	73	91.25	0.409
Inadequate feeding:					
-Present	37	46.25	33	41.25	0.639
-Absent	43	53.75	47	58.75	0.039

4. DISCUSSION

There are basic challenges and debates in treating neonatal hypoglycemia since the physiologic transitional changes to autonomous glucose regulation may occur during the same time period as the onset of inherited and acquired pathologic types of hypoglycemia.^[16] Therefore, in order to identify the exact cause and perform prompt interventions to prevent irreversible brain damage, a careful approach to the neonate with hypoglycemia is essential.^[17]

In this study gestational diabetes found to be significantly associated with symptomatic hypoglycemia, this is due to the fact maternal hyperglycemic state can lead to excessive glucose crosses the placenta and fetus develop hyperinsulinemia to adapt this condition. Comparable findings obtained from Takeshi Arimitsu et $al^{[18]}$ and Yu-Shao Chen et al.^[19]

On the other hand; small for gestational age found in this study to be risk factor for asymptomatic hypoglycemia, as hypoglycemia in these babies may be caused by abnormally high insulin levels and a lack of counterregulatory hormone response. Hypoglycemic SGA newborns also have low amounts of glucagon, another counter-regulatory hormone. These mechanisms are adapted differently from neonate to other therefore sometimes it occurred asymptomatically. Lin-Yu Wang

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et al had closed results.^[20] In same way; the study found that low birth weight is a risk factor for asymptomatic hypoglycemia as neonate with low birth weight had increased metabolic demands and limited energy reserves, which is runs with Babu Francis V. J. et al study findings.^[21] Respiratory distress syndrome found in this study to be significantly more frequent with asymptomatic hypoglycemia, this is due to hypoglycemia increase the counter-regulatory hormones, which is lead to increase in isocapnic ventilation, and increase in the hypoxic ventilatory response, this result consistent with Kiran Bhojraj Bhaisare et al study results.^[22]

This study has certain limitations because it is retrospective in nature which, there may be selection bias or insufficient data collection. Additionally, small sample size and depending on only one hospital can restrict its generalizability. Lack of specific data on several maternal and neonatal characteristics or possible confounders could compromise the validity of the study.

5. CONCLUSION

According to the study findings; maternal GDM can cause more symptomatic hypoglycemia, while SGA, LBW, and RDS can cause asymptomatic hypoglycemia.

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Conflict of intertest

About this study, the authors disclose no conflicts of interest.

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